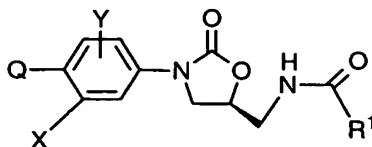


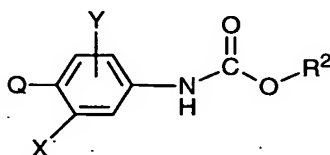
## CLAIMS

1. A novel process for preparing a compound of formula I



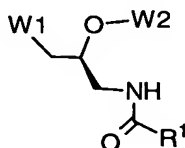
I

- 5 or a salt thereof, which comprises reacting a N-aryl -O-alkylcarbamate of formula II



II

or a salt thereof, with a compound of formula III



III

10

or a salt thereof, in the presence of a lithium cation, a base and a nucleophile, wherein X and Y are independently H or F;

W1 is Cl, Br, or -OS(O)<sub>2</sub>-R;

W2 is H or -C(O)-R<sub>1</sub>;

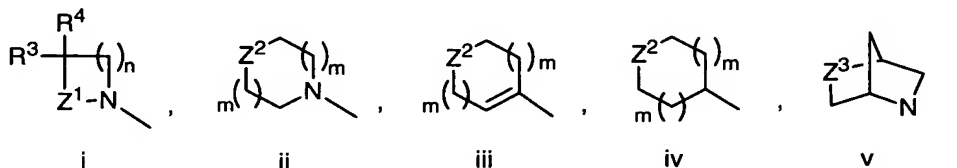
- 15 R is aryl or alkyl, the alkyl optionally being substituted by one or more F, Cl, Br, or I;

R<sup>1</sup> is CH<sub>3</sub>, optionally substituted by one to three fluorine or chlorine atoms;

R<sup>2</sup> is cycloalkyl, phenyl, -CH<sub>2</sub>-phenyl, C<sub>2-6</sub>alkenyl, or C<sub>1-12</sub>alkyl optionally substituted by one to three of F, Br, Cl, -O-C<sub>1-6</sub>alkyl, and NR<sup>2a</sup>R<sup>2b</sup>;

Each R<sup>2a</sup> and R<sup>2b</sup> is independently H or C<sub>1-4</sub>alkyl;

- 20 Q is structure i, ii, iii, iv, or iv:



or Q and X taken together are dihydropyrrolidine, optionally substituted with R<sup>5</sup>;

Z<sup>1</sup> is CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>, CH(OH)(CH<sub>2</sub>)<sub>p</sub>, or C(O);

$Z^2$  is S, SO, SO<sub>2</sub>, O, or N(R<sup>6</sup>);

$Z^3$  is S, SO, SO<sub>2</sub> or O;

$R^3$  is H or CH<sub>3</sub>;

$R^4$  is

- 5           a)     H,
- b)     HO,
- c)     C<sub>1-3</sub>alkyl;
- d)     C<sub>1-4</sub>alkoxy,
- e)     R<sup>7</sup>OCH<sub>2</sub>=C(O)NH-,
- 10          f)     R<sup>8</sup>OC(O)NH-,
- g)     C<sub>1-3</sub>alkyl-OC(O)-,
- h)     HOCH<sub>2</sub>-,
- i)     CH<sub>3</sub>ONH,
- j)     CH<sub>3</sub>C(O)-,
- 15          k)     CH<sub>3</sub>C(O)CH<sub>2</sub>-,
- l)     CH<sub>3</sub>C(OCH<sub>2</sub>CH<sub>2</sub>O)-, or
- m)     CH<sub>3</sub>C(OCH<sub>2</sub>CH<sub>2</sub>O)CH<sub>2</sub>-;

$R^3$  and  $R^4$  taken together with the carbon atom to which they are attaching form C(O), or C(=NR<sup>9</sup>);

20     $R^5$  is

- a)     CH<sub>3</sub>C(O)-,
- b)     HC(O)-,
- c)     Cl<sub>2</sub>CHC(O)-,
- d)     HOCH<sub>2</sub>C(O)-,
- 25          e)     CH<sub>3</sub>SO<sub>2</sub>-,
- f)     F<sub>2</sub>CHC(O)-,
- g)     H<sub>3</sub>CC(O)OCH<sub>2</sub>C(O)-,
- h)     HC(O)OCH<sub>2</sub>C(O)-,
- i)     R<sup>10</sup>C(O)OCH<sub>2</sub>C(O)-,
- 30          j)     H<sub>3</sub>CCHCH<sub>2</sub>OCH<sub>2</sub>C(O)-, or
- k)     benzylOCH<sub>2</sub>C(O)-;

$R^6$  is

- a)     H,

- b)  $C_{1-6}$ alkyl, optionally substituted with one or more OH, CN, or halo,
- c)  $-(CH_2)_h$ -aryl,
- d)  $-COR^{11}$ ,
- e)  $-COOR^{12}$ ,
- 5 f)  $-CO-(CH_2)_h-COR^{11}$ ,
- g)  $-SO_2-C_{1-6}$ alkyl,
- h)  $-SO_2-(CH_2)_h$ -aryl, or
- i)  $-(CO)_i$ -Het;

$R^7$  is H,  $CH_3$ , benzyl, or  $CH_3C(O)-$ ;

10  $R^8$  is  $(C_{1-3})$ alkyl, aryl, or benzyl;

$R^9$  is

- a) HO-
- b)  $CH_3O-$
- c)  $H_2N-$
- 15 d)  $CH_3OC(O)O-$ ,
- e)  $CH_3C(O)OCH_2C(O)O-$ ,
- f) aryl- $CH_2OCH_2C(O)O-$ ,
- g)  $HO(CH_2)_2O-$ ,
- h)  $CH_3OCH_2O(CH_2)_2O-$ , or
- 20 i)  $CH_3OCH_2O-$ ;

$R^{10}$  is:

- a)  $CH_3-$ ,
- b)  $HOCH_2-$ ,
- c) phenyl-NH-, or
- 25 d)  $(CH_3)_2N-CH_2-$ ;

$R^{11}$  is

- a) H,
- b)  $C_{1-6}$  alkyl, optionally substituted with one or more OH, CN, or halo,
- c)  $-(CH_2)_h$ -aryl, or
- 30 d)  $-(CH_2)_h-OR^{13}$ ;

$R^{12}$  is

- a)  $C_{1-6}$  alkyl, optionally substituted with one or more OH, CN, or halo,

b)  $-(CH_2)_h$ -aryl, or

c)  $-(CH_2)_h$ -OR<sup>13</sup>;

R<sup>13</sup> is

a) H,

5 b) C<sub>1-6</sub> alkyl,

c)  $-(CH_2)_h$ -aryl, or

d)  $-CO(C_{1-6} \text{ alkyl})$ ;

aryl is phenyl, pyridyl or naphthyl;

at each occurrence, aryl or phenyl may be optionally substituted with one or more F,

10 Cl, Br, I, CN, OH, SH, C<sub>1-6</sub> alkyl, OC<sub>1-6</sub> alkyl, or SC<sub>1-6</sub> alkyl, or OC(O)CH<sub>3</sub>;

het is 5- to 10-membered heterocyclic rings having one or more oxygen, nitrogen, and sulfur atoms;

h is 1, 2, 3, or 4;

i is 0 or 1;

15 m is 0 or 1;

n is 1, 2, or 3; and

p is 0, 1, or 2.

2. The process of claim 1 wherein R<sup>1</sup> is  $-CH_3$ .

20

3. The process of claim 1 wherein R<sup>1</sup> is  $-CHCl_2$ .

4. The process of claim 1 wherein R<sup>2</sup> is methyl, ethyl, propyl, isopropyl, 2,2,2-trifluoroethyl, isobutyl, 2-ethoxyethyl, 2-(N,N-dimethylamino)ethyl, 2-(N,N-diethylamino)ethyl, 2,2,2-trichloroethyl, isopropenyl, phenyl, p-tolyl, 2-methoxyphenyl or 4-methoxyphenyl.

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5. The process of claim 1 wherein R<sup>2</sup> is isobutyl.

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6. The process of claim 1 wherein R<sup>2</sup> is benzyl.

7. The process of claim 1 wherein Q is structure ii, wherein Z<sup>2</sup> is O or SO<sub>2</sub>.

8. The process of claim 1 wherein Q is a structure iii or iv, wherein Z<sup>2</sup> is O or SO<sub>2</sub>.
9. The process of claim 1 wherein Q is a structure ii, wherein Z<sup>2</sup> is N(R<sup>6</sup>).
10. The process of claim 9 wherein R<sup>6</sup> is COR<sup>11</sup>, wherein R<sup>11</sup> is C<sub>1-6</sub>alkyl optionally substituted with one or more OH.
11. The process of claim 1 wherein the base has pK<sub>DMSO</sub> greater than 12.
12. The process of claim 1 wherein the base is alkoxide, C<sub>1-4</sub> alky carbanion, conjugate base of a carbamate, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0] non-5-ene, lithium diisopropylamide, lithium dicyclohexylamide, lithium hexamethyldisilazide, or lithium amide.
13. The process of claim 1 wherein the base is alkoxide having one to five carbon atoms.
14. The process of claim 1 wherein the base is tertiary-amylate.
15. The process of claim 1 wherein the base is tertiary-butoxide.
16. The process of claim 1 wherein the nucleophile is alkoxide.
17. The process of claim 1 wherein the nucleophile is methoxide, ethoxide, isopropoxide, isobutoxide, 2-ethoxyethyl, 2-(N,N-dimethylamino)ethoxide, 2,2,2-trichloroethoxide, or 2,2,2-trifluoroethoxide.
18. The process of claim 1 wherein W1 is Cl.
19. The process of claim 1 wherein W1 is Br.

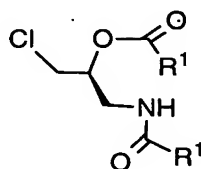
20. The process of claim 1 wherein W1 is  $-\text{OS}(\text{O})_2\text{-R}$ .

21. The process of claim 1 wherein W2 is H.

22. The process of claim 1 wherein W2 is  $-\text{C}(\text{O})\text{-R}_1$ .

23. The process of claim 1 wherein the reaction is conducted in a solvent system comprising THF and acetonitrile.

24. An intermediate of formula IV useful for the process of claim 1

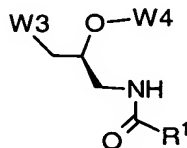


IV

wherein  $\text{R}^1$  is  $\text{CHCl}_2$ ,  $\text{CHBr}_2$ ,  $\text{CH}_2\text{Cl}$ ,  $\text{CH}_2\text{Br}$ ,  $\text{CCl}_3$ ,  $\text{CBr}_3$ ,  $\text{CHF}_2$ ,  $\text{CHF}_2$ , or  $\text{CF}_3$ .

25. An intermediate of claim 24 wherein  $\text{R}^1$  is  $\text{CHCl}_2$ .

26. An intermediate of the formula V



V

wherein

W3 is  $-\text{OS}(\text{O})_2\text{-R}$ ;

W4 is H or  $-\text{C}(\text{O})\text{-R}_1$ ;

R is aryl or alkyl, the alkyl is optionally substituted by one or more F, Cl, Br, or I, and the aryl is optionally substituted with one or more F, Cl, Br, I, CN, OH,  $\text{NO}_2$ ,

SH,  $\text{C}_{1-6}$  alkyl,  $\text{OC}_{1-6}$  alkyl, or  $\text{SC}_{1-6}$  alkyl, or  $\text{OC}(\text{O})\text{CH}_3$ ; and

$\text{R}^1$  is  $\text{CH}_3$ , optionally substituted by one to three fluorine or chlorine atoms.